

Complete Summary

GUIDELINE TITLE

Glaucoma. Diagnosis and management of chronic open angle glaucoma and ocular hypertension.

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Center for Acute Care. Glaucoma. Diagnosis and management of chronic open angle glaucoma and ocular hypertension. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Apr. 37 p. (NICE clinical guideline; no. 85).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
 METHODOLOGY - including Rating Scheme and Cost Analysis
 RECOMMENDATIONS
 EVIDENCE SUPPORTING THE RECOMMENDATIONS
 BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
 CONTRAINDICATIONS
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 IMPLEMENTATION OF THE GUIDELINE
 INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
 CATEGORIES
 IDENTIFYING INFORMATION AND AVAILABILITY
 DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

- Chronic open angle glaucoma (COAG)
- Ocular hypertension (OHT)

GUIDELINE CATEGORY

Counseling
 Diagnosis
 Evaluation
 Management
 Treatment

CLINICAL SPECIALTY

Family Practice
Geriatrics
Internal Medicine
Ophthalmology

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Patients
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide guidance on the diagnosis and treatment of chronic open angle glaucoma (COAG) and ocular hypertension (OHT)

TARGET POPULATION

- Adults (18 and older) with a diagnosis of chronic open angle glaucoma or ocular hypertension and those with chronic open angle glaucoma or ocular hypertension associated with pseudoexfoliation or pigment dispersion
- Populations who have a higher prevalence of glaucoma and may have worse clinical outcomes, including people with a family history of glaucoma, younger people (<50 years), and people who are of black African or black Caribbean descent

Note: This guideline does not cover patients under the age of 18 years. In addition, the guideline does not cover patients with secondary glaucoma (for example neovascular or uveitic) except for those described above, those with, or at risk of, primary or secondary angle closure glaucoma and adults with primary congenital, infantile, or childhood glaucoma.

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Intraocular pressure (IOP) measurement using Goldmann applanation tonometry (slit lamp mounted)
2. Central corneal thickness (CCT) measurement
3. Peripheral anterior chamber configuration and depth assessments using gonioscopy
4. Visual field measurement using standard automated perimetry (central thresholding test)
5. Optic nerve assessment, with dilatation, using stereoscopic slit lamp biomicroscopy with fundus examination
6. Adopting guidance to reduce risk of transmitting infection
7. Use of Van Herick's peripheral anterior chamber assessment as an alternative to gonioscopy

8. Obtaining an optic head nerve head image for baseline documentation
9. Ensuring appropriate records are made available at each clinical episode to all healthcare professionals involved in a person's care
10. Use of alternative methods of assessment as appropriate
11. Ensuring that all machines and measurement instruments are calibrated regularly
12. Repeat of diagnostic assessments at each monitoring assessment as appropriate
13. Monitoring at regular intervals people with ocular hypertension (OHT) or suspected chronic open angle glaucoma (COAG) recommended to receive medication, according to their risk of conversion to COAG
14. Monitoring at regular intervals people with COAG according to their risk of progression to sight loss

Treatment/Management/Counseling

1. Beta-blockers
2. Prostaglandin analog
3. Carbonic anhydrase inhibitor
4. Sympathomimetic
5. Mitomycin C or 5-fluorouracil augmentation
6. Laser trabeculoplasty or cyclodiode laser treatment
7. Surgery with pharmacological augmentation
8. Organization of care
9. Provision of information pertinent to patient's condition
10. Discussing risks and benefits of stopping treatment

MAJOR OUTCOMES CONSIDERED

- Prevalence of blindness attributed to glaucoma
- Progression of chronic open angle glaucoma (COAG)
- Conversion to COAG in ocular hypertensive patients
- Symptom improvement
- Quality of life
- Adverse effects of pharmacological treatments
- Postoperative complications of surgical and laser treatments

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
 Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Acute Care on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Clinical Literature Search

The aim of the literature search was to find 'evidence within the published literature', to answer the clinical questions identified. Clinical databases were searched using filters (or hedges), using relevant medical subject headings and free-text terms. Non-English language studies and abstracts were not reviewed.

Each database was searched up to 04 August 2008 (Week 32). One initial search was performed and then two update searches nearer the end of guideline development period. No papers after this date were considered.

The search strategies can be found in Appendix C in the full version of the guideline.

The following databases were searched:

- The Cochrane Library up to Issue 3 2008
- Medline 1950-2008 (OVID)
- Embase 1980-2008 (OVID)
- Cinahl 1982-2008 (Dialog Datastar and later NLH Search 2.0)
- PsycINFO 1800s-2008 (NLH Search 2.0)
- MED 1985-2008 (NLH Search 2.0)
- Health economic and evaluations database (HEED) up to August 2008

There was no systematic attempt to search for grey literature or unpublished literature although all stakeholder references were followed up. Guidelines and reports were searched for via relevant websites including those listed below.

- American Academy of Ophthalmology (<http://www.ao.org/>)
- Constituent websites of the Guidelines International Network (<http://www.g-i-n.net/>)
- International Council of Ophthalmology Guidelines (<http://www.icoph.org/guide/guideintro.html>)
- International Glaucoma Association (<http://www.glaucoma-association.com/>)
- National Guideline Clearinghouse (<http://www.guideline.gov/>)
- National Institute for Health and Clinical Excellence (NICE) (<http://www.nice.org.uk/>)
- National Institutes of Health Consensus Development Program (<http://consensus.nih.gov/>)
- National Library for Health (<http://www.library.nhs.uk/>)
- National Library for Health Eyes and Vision Specialist Library (<http://www.library.nhs.uk/eyes/>)
- NHS Connecting for Health Do Once and Share Glaucoma project (<http://www.doasglaucoma.org/>)
- Royal College of Ophthalmologists (<http://www.rcophth.ac.uk/>)

Economic Literature Search

Published economic evidence were obtained from a systematic search of the following databases:

- The Cochrane Library up to Issue 3 2008
- Medline 1950-2008 (OVID)
- Embase 1980-2008 (OVID)
- Health economic and evaluations database (HEED) up to August 2008

The information specialists used the same search strategy as for the clinical questions, using an economics filter in the place of a systematic review or randomised controlled trial filter. Each database was searched from its start date up to August 2008. Papers identified after this date were not considered. Search strategies can be found in Appendix C in the full version of the guideline.

Each search strategy was designed to find any applied study estimating the cost or cost-effectiveness of an included intervention. A health economist reviewed the abstracts. Relevant references in the bibliographies of reviewed papers were also identified and reviewed.

NUMBER OF SOURCE DOCUMENTS

107 studies met inclusion criteria.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels Of Evidence for Studies of Accuracy of Diagnostic Tests

Ia: Systematic review with homogeneity^a of level-1 studies^b

Ib: Level-1 studies^b

II: Level-2 studies^c; Systematic reviews of level-2 studies

III: Level-3 studies^d; Systematic reviews of level-3 studies

IV: Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or 'first principles'

^a Homogeneity indicates there are none or minor variations in the directions and degrees of results between individual studies included in the systematic review

^b Level-1 studies:

- Use a blind comparison of the test with a reference standard (gold standard)
- Are conducted in a sample of patients that reflects the population to whom the test would apply

^c Level-2 studies have only one of the following:

- Narrow population (sample does not reflect the population to whom the test would apply)
- A poor reference standard (where tests are not independent)
- The comparison between the test and reference standard is not masked
- A case-control study design

^d Level-3 studies have two or three of the above features

Levels of Evidence for Intervention Studies

1++ High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias

1+ Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

1- Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

2++ High-quality systematic reviews of case-control or cohort studies

High-quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal

2+ Well-conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal

2- Case-control or cohort studies with a high risk of confounding bias, or chance and a significant risk that the relationship is not causal

3 Non-analytic studies (For example, case reports, case series)

4 Expert opinion, formal consensus

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Randomized Controlled Trials
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Acute Care (NCC-AC) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Service Provision

The kappa weighted statistic or intraclass correlation coefficient was selected as the outcome measure of agreement between healthcare professionals for diagnosis, monitoring and treatment decisions. Most studies (randomized controlled trials [RCTs] or observational) used an agreement scale (see Table 2-3 in the full version of the original guideline) to compare the reported statistics. The Guideline Development Group (GDG) felt that only agreement levels of moderate or greater should be considered as adequate evidence of clinical agreement because lower levels of agreement would not provide sufficient consistency of quality or continuity of care for a service delivered by different healthcare provider groups.

GRADE

Outcome evidence was written up using the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group (<http://www.gradeworkinggroup.org/>). The software developed by the working group, GRADEpro, was used to assess pooled outcome data using individual study quality assessments and results from meta-analysis.

Each outcome was examined for the following quality elements listed in Table 2-4 and each graded using the quality levels listed in Table 2-5 in the full version of the original guideline. Footnotes were used to describe reasons for grading a quality element as having serious or very serious problems and then an overall quality of evidence for each outcome was applied by selecting from the options listed in Table 2-6 in the full version of the original guideline.

Results were presented as two separate tables. The clinical study characteristics table includes details of the quality assessment and the clinical summary outcome table includes pooled outcome data and an absolute measure of intervention effect calculated in the GRADEpro software using the control event rate and the risk ratio values from the meta-analysis.

The GRADE toolbox is currently designed only for randomized controlled trials and observational studies but we adapted the quality assessment elements and outcome presentation for diagnostic accuracy studies and service provision.

NICE Economic Profile

Since GRADE was not originally designed for economic evidence, the NICE economic profile has been used to present cost and cost-effectiveness estimates from published studies or analyses conducted for the guideline. As for the clinical evidence, the economic evidence has separate tables for the quality assessment and for the summary of results. The quality assessment is based on two criteria — limitations and applicability (Table 2-7) and each criterion is graded using the levels in Table 2-8 and Table 2-9 of the full version of the original guideline.

An overall score of the evidence is not given as it is not clear how the quality elements could be summarised into a single quality rating.

A summary of results is presented for each study including:

- Incremental cost
- Incremental effectiveness
- Incremental cost-effectiveness ratio
- Uncertainty

Clinical Literature Reviewing Process

References identified by the systematic literature search were screened for appropriateness by title and abstract by an information scientist and systematic reviewer. Studies were selected that reported one or more of the outcomes listed in section 2.3 of the full version of the original guideline document and in the "Major Outcomes" section of this summary. Selected studies were ordered and assessed in full by the NCC-AC team using agreed inclusion/exclusion criteria specific to the guideline topic, and using NICE methodology quality assessment checklists appropriate to the study design. Further references suggested by the guideline development group were assessed in the same way. Not enough data was available from RCTs for serious adverse events related to pharmacological interventions. Consequently, an additional literature review of observational data was performed to supplement the RCT evidence.

Economic Literature Reviewing Process

Economic studies identified in the systematic search were excluded from the review if:

- The study did not contain any original data on cost or cost-effectiveness (that is, it was a review or a clinical paper)
- The study population did not comply with the inclusion criteria as established in the clinical effectiveness review methods
- The analysis was not incremental and was not described adequately to allow incremental analysis (so studies reporting only average cost-effectiveness ratios were excluded unless they provided data to allow the calculation of incremental cost-effectiveness ratios)
- The study was a non-UK cost-analysis
- The study was a letter or written in a foreign language
- The estimates of treatment effectiveness in the economic study were obtained from a follow-up less than six months (see section 2.3 of the full version of the original guideline document)

Included papers were reviewed by a health economist. In the evidence tables, costs are reported as in the paper. However, where costs were in a currency other than pounds sterling, the results were converted into pounds sterling using the appropriate purchasing power parity for the study year.

Studies from all over the world were included in the review, however, overseas studies were used with caution since resource use and especially unit costs vary considerably. Particular caution was applied to studies with predominantly private health insurance (for example, USA or Switzerland) where unit costs may be much higher than in the UK and to developing countries where costs may be much lower.

Each study was categorised as one of the following: cost analysis, cost-effectiveness analysis, cost-utility analysis (that is, cost-effectiveness analysis with effectiveness measured in terms of quality-of-life years [QALYs]), or cost consequences analysis. No 'cost benefit analyses' (studies that put a monetary value on health gain) were found.

Models are analogous to systematic reviews because they pool evidence from a number of different studies and therefore if well-conducted they should out-rank studies based on a single RCT. Statistical significance is not usually applicable to models and uncertainty is explored using sensitivity analysis instead. Hence the results reported in economic GRADE tables, evidence tables and write-up may not necessarily imply statistical significance.

Cost-Effectiveness Modelling

The details of the economic model are described in Appendix F of the full version of the original guideline document.

Methods of Combining Studies

Where possible, meta-analyses were conducted to combine the results of studies for each clinical question using Cochrane Review Manager software. Fixed-effects (Mantel-Haenszel) techniques were used to calculate risk ratios (relative risk) for the binary outcomes: number of patients with visual field progression, number of patients with an acceptable or unacceptable intraocular pressure (IOP) or numbers of adverse events, and the continuous outcome for change in IOP from baseline was analysed using an inverse variance method for pooling weighted mean differences. When combining data for number of patients with visual field progression it was acknowledged that there may be limitations as it is difficult to standardise this outcome when each study has defined and measured visual field progression differently. Statistical heterogeneity was assessed by considering the chi-squared test for significance at $p < 0.05$ and an I-squared of $\geq 25\%$ to indicate significant heterogeneity.

Where significant heterogeneity was present a number of possible predefined differences were explored including chronic open angle glaucoma (COAG) population and study design (open label or masked) by doing subgroup analyses. Assessments of potential differences in effect between subgroups were based on the chi-squared tests for heterogeneity statistics between subgroups. If no sensitivity analysis was found to completely resolve statistical heterogeneity then a random effects (DerSimonian and Laird) model was employed to provide a more conservative estimate of the effect.

For the outcome change in IOP from baseline some studies did not report standard deviations or provided only baseline and end point data. The methods outlined in section 7.7.3 of the Cochrane Handbook (February 2008) 'Data extraction for continuous outcomes' were applied if p values and confidence intervals had been reported. If these statistical measures were not available then the methods described in section 16.1.3 of the Cochrane Handbook (February 2008) 'Missing standard deviations' were applied. Detailed data provided for IOP at baseline, end point and change from another study in the comparison were used as inputs for the calculations.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Acute Care (NCC-AC) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Â Development of the Recommendations

Over the course of the guideline development process, the Guideline Development Group (GDG) was presented with the following:

- Evidence tables of the clinical and economic evidence reviewed. All evidence tables are in appendix D in the full version of the original guideline document
- Forest plots of meta-analyses (appendix E in the full version of original guideline)
- A description of the methods and results of the cost-effectiveness analysis (appendix F in the full version of the original guideline)

Recommendations were drafted on the basis of this evidence wherever it was available.

When clinical and economic evidence was poor or absent, the GDG proposed recommendations based on their expert opinion. The GDG added supporting recommendations whenever it was necessary in order to improve clinical practice. The supporting recommendations were not derived from clinical questions and they were based on GDG expert opinion.

The development of the recommendations required several steps:

- A first draft of all recommendations was circulated to the GDG using an internet based system. NCC-AC staff facilitated a structured discussion considering each recommendation so that GDG members could evaluate their own feedback in relation to other GDG members.
- NCC-AC staff modified the recommendations as a result of the discussion and in the light of NICE guidance on writing recommendations.
- The GDG was asked to independently feed back their comments on these modified recommendations to the NCC. This procedure allowed the NCC to verify the level of agreement between the GDG members.
- All GDG feedback was collated and circulated again to the GDG. The recommendations were then finalized.
- During the writing up phase of the guideline, the GDG could further refine each recommendation working in subgroups on each chapter.
- NCC-AC staff verified the consistency of all recommendations across the guideline.

The GDG then developed a care pathway algorithm according to the recommendations.

Prioritisation of Recommendations for Implementation

To assist users of the guideline in deciding the order in which to implement the recommendations, the GDG identified ten key priorities for implementation. The decision was made after discussion and voting by the GDG. They selected recommendations that would:

- Have a high impact on outcomes that are important to patients
- Have a high impact on reducing variation in care and outcomes
- Lead to a more efficient use of National Health Service (NHS) resources
- Promote patient choice
- Promote equalities

In doing this the GDG also considered which recommendations were particularly likely to benefit from implementation support. They considered whether a recommendation:

- Requires changes in service delivery
- Requires retraining of professionals or the development of new skills and competencies
- Affects and needs to be implemented across various agencies or settings (complex interactions)
- May be viewed as potentially contentious, or difficult to implement for other reasons

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Most of the economic evidence of this guideline derives from original cost-effectiveness analyses carried out by the National Collaborating Centre for Acute Care (NCC-AC). The main cost-effectiveness analysis was carried out to answer the clinical questions on treatment of patients with ocular hypertension (OHT) and chronic open angle glaucoma (COAG) suspects (see Chapter 7 of the full version of the original guideline document), and the clinical question on treatment of patients with COAG (see Chapter 8 of the full version of the original guideline). Throughout the guideline this analysis is referred to as the 'NCC-AC model'. A further cost analysis was carried out to answer the clinical questions on diagnosis and monitoring measurements (see Chapters 4 and 5 of the full version of the original guideline). Throughout the guideline this analysis is referred to as 'NCC-AC cost analysis'.

Conclusions

- Treating all patients with OHT is not cost-effective.

- It is cost-effective to treat only OHT patients with IOP > 25 to 32 mm Hg and central corneal thickness (CCT) 555 to 590 micrometers with a beta-blocker until the age of 60 and OHT patients with IOP >21 and CCT ≤555 micrometers with a prostaglandin analogue until the age of 80.

It is always cost-effective to treat COAG patients. However, trabeculectomy is cost-effective only when progression of visual field defect for Early COAG patients is >0.18 decibel (dB)/per year — which is to say in the presence of any detectable progression. Trabeculectomy becomes more and more cost-effective the more advanced the stage of COAG.

Refer to Appendix F of the full version of the original guideline document for details of the cost-effectiveness analysis.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline was validated through two consultations.

1. The first draft of the guideline (The full guideline, National Institute for Clinical Excellence [NICE] guideline and Quick Reference Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG)
2. The final consultation draft of the full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments

The final draft was submitted to the Guideline Review Panel for review prior to publication.

The first draft of this guideline was posted on the NICE website for consultation between 29th September - 24th November 2008 and registered stakeholders were invited to comment. The GDG responded to comments and an amended version of the guideline was produced.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Acute Care on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Diagnosis

At diagnosis offer all people who have chronic open angle glaucoma (COAG), who are suspected of having COAG or who have ocular hypertension (OHT) all of the following tests:

- Ocular pressure (OP) measurement using Goldmann applanation tonometry (slit lamp mounted)
- Central corneal thickness (CCT) measurement
- Peripheral anterior chamber configuration and depth assessments using gonioscopy
- Visual field measurement using standard automated perimetry (central thresholding test)
- Optic nerve assessment, with dilatation, using stereoscopic slit lamp biomicroscopy with fundus examination

Adopt professional*/Department of Health** guidance to reduce the risk of transmitting infective agents via contact tonometry or gonioscopy.

* Royal College of Ophthalmologists (<http://www.rcophth.ac.uk/>) and the Medicines and Healthcare products Regulatory Agency (www.mhra.gov.uk).

** See <http://www.advisorybodies.doh.gov.uk/>.

Use Van Herick's peripheral anterior chamber depth assessment as an alternative to gonioscopy if clinical circumstances rule out gonioscopy (for example, when people with physical or learning disabilities are unable to participate in the examination).

Obtain an optic nerve head image at diagnosis for baseline documentation.

Ensure that all of the following are made available at each clinical episode to all healthcare professionals involved in a person's care:

- Records of all previous tests and images relevant to COAG and OHT assessment
- Records of past medical history which could affect drug choice
- Current systemic and topical medication
- Glaucoma medication record
- Drug allergies and intolerances

Use alternative methods of assessment if clinical circumstances rule out the use of standard methods of assessment (for example, when people with physical or learning disabilities are unable to participate in the examination).

Ensure that all machines and measurement instruments are calibrated regularly according to the manufacturer's instructions.

Monitoring

Offer Goldmann applanation tonometry (slit lamp mounted) to all people with COAG, who are suspected of having COAG or who have OHT at each monitoring assessment.

Repeat CCT measurement as necessary (for example, following laser refractive surgery or at onset or progression of corneal pathology).

Offer Van Herick's peripheral anterior chamber depth assessment to all people with COAG, who are suspected of having COAG or who have OHT at each monitoring assessment.

Repeat gonioscopy when clinically indicated (for example, where a previous examination has been inconclusive or where there is suspicion of a change in clinical status of the anterior chamber angle).

Offer standard automated perimetry (central thresholding test) to all people who have established COAG and those suspected of having visual field defects who are being investigated for possible COAG. People with diagnosed OHT and those suspected of having COAG whose visual fields have previously been documented by standard automated perimetry as being normal may be monitored using supra-threshold perimetry (see tables below for recommended monitoring intervals).

Where a defect has previously been detected use the same visual field measurement strategy for each visual field test.

Offer stereoscopic slit lamp biomicroscopic examination of the optic nerve head to all people with COAG, who are suspected of having COAG or who have OHT at monitoring assessments (see tables below for recommended monitoring intervals).

When a change in optic nerve head status is detected by stereoscopic slit lamp biomicroscopic examination, obtain a new optic nerve head image for the person's records to provide a fresh benchmark for future assessments.

When an adequate view of the optic nerve head and surrounding area is unavailable at a monitoring visit, people undergoing stereoscopic slit lamp biomicroscopy should have their pupils dilated before the assessment.

Monitor at regular intervals people with OHT or suspected COAG recommended to receive medication according to their risk of conversion to COAG (see table below).

Table: Monitoring Intervals for People with OHT or Suspected COAG Who Are Recommended to Receive Medication

Clinical Assessment		Monitoring Intervals (months)		
IOP at target ^a	Risk of conversion to COAG ^b	Outcome ^c	IOP alone ^d	IOP, optic nerve head and visual field
Yes	Low	No change in treatment plan	Not applicable	12 to 24

Clinical Assessment		Monitoring Intervals (months)		
IOP at target ^a	Risk of conversion to COAG ^b	Outcome ^c	IOP alone ^d	IOP, optic nerve head and visual field
Yes	High	No change in treatment plan	Not applicable	6 to 12
No	Low	Review target IOP or change treatment plan	1 to 4	6 to 12
No	High	Review target IOP or change treatment plan	1 to 4	4 to 6

^a Person is treated and IOP is at or below target. If IOP cannot be adequately controlled medically, refer to consultant ophthalmologist.
^b To be clinically judged in terms of age, IOP, CCT, appearance and size of optic nerve head.
^c For change of treatment plan refer to treatment recommendations.
^d For people started on treatment for the first time check IOP 1 to 4 months after start of medication.

Discuss the benefits and risks of stopping treatment with people with OHT or suspected COAG who have both:

- A low risk of ever developing visual impairment within their lifetime
- An acceptable IOP

If a person decides to stop treatment following discussion of the perceived risks of future conversion to COAG and sight loss, offer to assess their IOP in 1 to 4 months' time with further monitoring if considered clinically necessary.

In people with OHT or suspected COAG who are not recommended to receive medication, assess IOP, optic nerve head and visual field at the following intervals:

- Between 12 and 24 months if there is a low risk of conversion to COAG
- Between 6 and 12 months if there is a high risk of conversion to COAG

If no change in the parameters has been detected after 3 to 5 years (depending on perceived risk of conversion), or before if confirmed normal, the person should be discharged from active glaucoma care to community optometric care.

At discharge advise people who are not recommended for treatment and whose condition is considered stable to visit their primary care optometrist annually so that any future changes in their condition can be detected.

Monitor at regular intervals people with COAG according to their risk of progression to sight loss (see table below).

Table: Monitoring Intervals for People with COAG

Clinical Assessment		Monitoring Intervals (months)		
IOP at target ^a	Progression ^b	Outcome ^c	IOP alone ^d	IOP, optic nerve head and visual field
Yes	No ^e	No change in treatment plan	Not applicable	6 to 12
Yes	Yes	Review target IOP and change treatment plan	1 to 4	2 to 6
Yes	Uncertain	No change in treatment plan	Not applicable	2 to 6
No	No ^e	Review target IOP or change treatment plan	1 to 4	6 to 12
No	Yes/uncertain	Change treatment plan	1 to 2	2 to 6

^a IOP at or below target.
^b Progression = increased optic nerve damage and/or visual field change confirmed by repeated test where clinically appropriate.
^c For change of treatment plan refer to treatment recommendations.
^d For people started on treatment for the first time check IOP 1 to 4 months after start of medication.
^e No = not detected or not assessed if IOP check only following treatment change.

Following full recovery from surgery or laser trabeculoplasty, restart monitoring according to IOP, optic nerve head appearance and visual field (see table above).

Treatment for People with OHT and Suspected COAG

Offer people with OHT or suspected COAG with high IOP treatment based on estimated risk of conversion to COAG using IOP, CCT and age (see table below).

Table: Treatment for People with OHT or Suspected COAG

CCT	More Than 590 Micrometres		555–590 Micrometres		Less Than 555 Micrometres		Any
Untreated IOP (mmHg)	>21 to 25	>25 to 32	>21 to 25	>25 to 32	>21 to 25	>25 to 32	>32
Age (years) ^a	Any	Any	Any	Treat until 60	Treat until 65	Treat until 80	Any
Treatment	No	No	No	BB ^b	PGA	PGA	PGA

CCT	More Than 590 Micrometres		555–590 Micrometres		Less Than 555 Micrometres		Any
	treatment	treatment	treatment				
<p>^a Treatment should not be routinely offered to people over the age threshold unless there are likely to be benefits from the treatment over an appropriate timescale. Once a person being treated for OHT reaches the age threshold for stopping treatment but has not developed COAG, healthcare professionals should discuss the option of stopping treatment. The use of age thresholds is considered appropriate only where vision is currently normal (OHT with or without suspicion of COAG) and the treatment is purely preventative. Under such circumstances the threat to a person's sighted lifetime is considered negligible. In the event of COAG developing in such a person then treatment is recommended.</p> <p>^b If beta-blockers (BB) are contraindicated offer a prostaglandin analogue (PGA).</p>							

Do not treat people with suspected COAG and normal IOP.

Check that there are no relevant comorbidities or potential drug interactions before offering medication.

Offer alternative pharmacological treatment (a prostaglandin analogue, beta-blocker, carbonic anhydrase inhibitor or sympathomimetic) to people with OHT or suspected COAG and high IOP who are intolerant of the current medication.

Offer alternative pharmacological treatment (a prostaglandin analogue, beta-blocker, carbonic anhydrase inhibitor or sympathomimetic) to treated people with OHT or suspected COAG whose IOP cannot be reduced sufficiently to prevent the risk of progression to sight loss. More than one agent may be needed concurrently to achieve target IOP.

Refer treated people with OHT or suspected COAG whose IOP cannot be reduced sufficiently to prevent the risk of progression to sight loss to a consultant ophthalmologist to discuss other options.

Offer a preservative-free preparation to people with OHT or suspected COAG and an allergy to preservatives only if they are at high risk of conversion to COAG (IOP more than 25 and up to 32 mmHg and CCT less than 555 micrometres, or IOP more than 32 mmHg).

Treatment for People with COAG

Check that there are no relevant comorbidities or potential drug interactions before offering medication.

Offer people newly diagnosed with early or moderate COAG, and at risk of significant visual loss in their lifetime, treatment with a prostaglandin analogue.

Offer people with advanced COAG surgery with pharmacological augmentation (mitomycin C [MMC] or 5-fluorouracil [5-FU])[#] as indicated. Offer them information on the risks and benefits associated with surgery.

Offer people who present with advanced COAG and who are listed for surgery interim treatment with a prostaglandin analogue.

Encourage people using the prescribed pharmacological treatment to continue with the same treatment unless:

- Their IOP cannot be reduced sufficiently to prevent the risk of progression to sight loss.
- There is progression of optic nerve head damage.
- There is progression of visual field defect.
- They are intolerant to the drug.

Check the person's adherence to their treatment and eye drop instillation technique in people with COAG whose IOP has not been reduced sufficiently to prevent the risk of progression to sight loss despite pharmacological treatment. If adherence and eye drop instillation technique are satisfactory offer one of the following:

- Alternative pharmacological treatment (a prostaglandin analogue, beta-blocker, carbonic anhydrase inhibitor or sympathomimetic); more than one agent may be needed concurrently to achieve target IOP
- Laser trabeculoplasty
- Surgery with pharmacological augmentation (MMC or 5-FU[#]) as indicated

If the pharmacological treatment option is chosen, after trying two alternative pharmacological treatments consider offering surgery with pharmacological augmentation (MMC or 5-FU[#]) as indicated or laser trabeculoplasty.

Offer surgery with pharmacological augmentation (MMC or 5-FU[#]) as indicated to people with COAG who are at risk of progressing to sight loss despite treatment. Offer them information on the risks and benefits associated with surgery.

Consider offering people with COAG who are intolerant to a prescribed medication:

- Alternative pharmacological treatment (a prostaglandin analogue, beta-blocker, carbonic anhydrase inhibitor or sympathomimetic) **or**
- A preservative-free preparation if there is evidence that the person is allergic to the preservative

After trying two alternative pharmacological treatments consider offering surgery with pharmacological augmentation (MMC or 5-FU[#]) as indicated or laser trabeculoplasty.

After surgery offer people with COAG whose IOP has not been reduced sufficiently to prevent the risk of progression to sight loss one of the following:

- Pharmacological treatment (a prostaglandin analogue, beta-blocker, carbonic anhydrase inhibitor or sympathomimetic); more than one agent may be needed concurrently to achieve target IOP
- Further surgery

- Laser trabeculoplasty or cyclodiode laser treatment

Offer people with COAG who prefer not to have surgery or who are not suitable for surgery:

- Pharmacological treatment (a prostaglandin analogue, beta-blocker, carbonic anhydrase inhibitor or sympathomimetic); more than one agent may be needed concurrently to achieve target IOP
- Laser trabeculoplasty or cyclodiode laser treatment.

Organization of Care

Refer people with suspected optic nerve damage or repeatable visual field defect, or both, to a consultant ophthalmologist for consideration of a definitive diagnosis and formulation of a management plan.

Diagnosis of OHT and suspected COAG and formulation of a management plan should be made by a suitably trained healthcare professional with:

- A specialist qualification (when not working under the supervision of a consultant ophthalmologist) **and**
- Relevant experience

Healthcare professionals involved in the diagnosis of OHT and COAG suspect status and preliminary identification of COAG should be trained in case detection and referral refinement and be able to identify abnormalities based on relevant clinical tests and assessments. They should understand the principles of diagnosis of OHT and COAG and be able to perform and interpret all of the following:

- Medical and ocular history
- Differential diagnosis
- Goldmann applanation tonometry (slit lamp mounted)
- Standard automated perimetry (central thresholding test)
- Central supra-threshold perimetry
- Stereoscopic slit lamp biomicroscopic examination of anterior segment
- Examination of the posterior segment using a slit lamp binocular indirect ophthalmoscopy
- Gonioscopy
- Van Herick's peripheral anterior chamber depth assessment
- CCT measurement

People with a diagnosis of OHT, suspected COAG or COAG should be monitored and treated by a trained healthcare professional who has all of the following:

- A specialist qualification (when not working under the supervision of a consultant ophthalmologist)
- Relevant experience
- Ability to detect a change in clinical status

Healthcare professionals involved in the monitoring and treatment of people with OHT, suspected COAG and established COAG should be trained to make management decisions on all of the following:

- Risk factors for conversion to COAG
- Coexisting pathology
- Risk of sight loss
- Monitoring and clinical status change detection (for example, visual field changes, stereoscopic slit lamp biomicroscopic examination of anterior segment and posterior segment)
- Pharmacology of IOP-lowering medications
- Treatment changes for COAG, COAG suspect status and OHT (with consideration given to relevant contraindications and interactions)

People with a confirmed diagnosis of OHT or suspected COAG and who have an established management plan may be monitored (but not treated) by a suitably trained healthcare professional with knowledge of OHT and COAG, relevant experience and ability to detect a change in clinical status. The healthcare professional should be able to perform and interpret all of the following:

- Goldmann applanation tonometry (slit lamp mounted)
- Standard automated perimetry (central thresholding test)
- Central supra-threshold perimetry (this visual field strategy may be used to monitor people with OHT or COAG suspect status when they have normal visual field)
- Stereoscopic slit lamp biomicroscopic examination of the anterior segment
- Van Herick's peripheral anterior chamber depth assessment
- Examination of the posterior segment using slit lamp binocular indirect ophthalmoscopy

Healthcare professionals who diagnose, treat or monitor people independently of consultant ophthalmologist supervision should take full responsibility for the care they provide.

Provision of Information

Offer people the opportunity to discuss their diagnosis, prognosis and treatment, and provide them with relevant information in an accessible format at initial and subsequent visits. This may include information on the following:

- Their specific condition (OHT, suspected COAG and COAG), its life-long implications and their prognosis for retention of sight
- That COAG in the early stages and OHT and suspected COAG are symptomless
- That most people treated for COAG will not go blind
- That once lost, sight cannot be recovered
- That glaucoma can run in families and that family members may wish to be tested for the disease
- The importance of the person's role in their own treatment – for example, the ongoing regular application of eye drops to preserve sight

- The different types of treatment options, including mode of action, frequency and severity of side effects, and risks and benefits of treatment, so that people are able to be active in the decision-making process
- How to apply eye drops, including technique (punctal occlusion and devices) and hygiene (storage)
- The need for regular monitoring as specified by the healthcare professional
- Methods of investigation during assessment
- How long each appointment is likely to take and whether the person will need any help to attend (for example, driving soon after pupil dilatation would be inadvisable)
- Support groups
- Compliance aids (such as dispensers) available from their General Practitioner or community pharmacist
- Letter of Vision Impairment (LVI), Referral of Vision Impairment (RVI) and Certificate of Vision Impairment (CVI) registration
- Driver and Vehicle Licensing Agency (DVLA) regulations

At the time of publication (April 2009), MMC and 5-FU did not have UK marketing authorisation for this indication. Informed consent should be obtained and documented. Both drugs should be handled with caution and in accordance with guidance issued by the Health and Safety Executive.

CLINICAL ALGORITHM(S)

The following algorithms can be found in the National Institute for Health and Clinical Excellence (NICE) [Quick Reference Guide](#) for Glaucoma (see also the "Availability of Companion Documents" field):

- Diagnosis of Ocular hypertension (OHT), suspected chronic open angle glaucoma (COAG) and COAG
- OHT pathway (monitoring and treatment for people with OHT and people with suspected COAG who have high intraocular pressure [IOP])
- Suspected COAG pathway (monitoring for people with suspected COAG and normal IOP)
- COAG pathway (monitoring and treatment for people with COAG)

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Recommendations are based on clinical and cost effectiveness evidence, and where this is insufficient, the Guideline Development Group (GDG) used all available information sources and experience to make consensus recommendations using nominal group technique.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Effective diagnosis, management, and treatment of chronic open angle glaucoma and ocular hypertension may prevent blindness.

POTENTIAL HARMS

- Side effects of treatment and interactions with other medications
- Incorrect treatment (absent or inadequate) leading to sight loss
- Incorrect diagnosis leading to sight loss
- Incorrect diagnosis leading to over treatment
- Potential for corneal burn is present if sterilising fluid remains or is allowed to dry on the prism with Goldmann applanation tonometry.
- There is a potential tradeoff between getting an accurate measurement of intraocular pressure and the risk of infection from contact tonometry.
- Gonioscopy is an invasive method, involves anaesthetic drops, and has the potential to damage the surface of the eye if used incorrectly.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Contraindications to dilatation should be observed and would include possible angle closure and an iris supported lens implant.
- Beta-blockers are contraindicated for patients with asthma, chronic obstructive pulmonary disease, bradycardia or heart block. In addition, they should not be used with calcium channel blockers because of the risk of inducing heart block.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance represents the view of the National Institute for Health and Clinical Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The National Institute for Health and Clinical Excellence (NICE) has developed tools to help organisations implement this guidance (listed below). These are available on the NICE website (<http://guidance.nice.org.uk/CG85>).

- Slides highlighting key messages for local discussion
- Costing tools:
 - Costing report to estimate the national savings and costs associated with implementation
 - Costing template to estimate the local costs and savings involved.
- Audit support to monitor local practice.

Key Priorities for Implementation

Diagnosis

- At diagnosis offer all people who have chronic open angle glaucoma (COAG), who are suspected of having COAG or who have ocular hypertension (OHT) all of the following tests: - intraocular pressure (IOP) measurement using Goldmann applanation tonometry (slit lamp mounted)
 - Central corneal thickness (CCT) measurement
 - Peripheral anterior chamber configuration and depth assessments using gonioscopy
 - Visual field measurement using standard automated perimetry (central thresholding test)
 - Optic nerve assessment, with dilatation, using stereoscopic slit lamp biomicroscopy with fundus examination
- Ensure that all of the following are made available at each clinical episode to all healthcare professionals involved in a person's care: - records of all previous tests and images relevant to COAG and OHT assessment
 - Records of past medical history which could affect drug choice
 - Current systemic and topical medication
 - Glaucoma medication record
 - Drug allergies and intolerances

Monitoring

- Monitor at regular intervals people with OHT or suspected COAG recommended to receive medication (see 'Treatment for people with OHT or suspected COAG' below and in the "Major Recommendations" section of this summary), according to their risk of conversion to COAG (see table 'Monitoring intervals for people with OHT or suspected COAG who are recommended to receive medication' in the "Major Recommendations" section of this summary).
- Monitor at regular intervals people with COAG according to their risk of progression to sight loss (see table 'Monitoring intervals for people with COAG' in the "Major Recommendations" section of this summary).

Treatment for People with OHT or Suspected COAG

- Offer people with OHT or suspected COAG with high IOP treatment based on estimated risk of conversion to COAG using IOP, CCT and age (see table 'Treatment for people with OHT or suspected COAG' in the "Major Recommendations" section of this summary).

Treatment for People with COAG

- Offer people newly diagnosed with early or moderate COAG, and at risk of significant visual loss in their lifetime, treatment with a prostaglandin analogue.
- Offer surgery with pharmacological augmentation (mitomycin C [MMC] or 5-fluorouracil [5-FU]) as indicated to people with COAG who are at risk of progressing to sight loss despite treatment. Offer them information on the risks and benefits associated with surgery.

Organisation of Care

- Refer people with suspected optic nerve damage or repeatable visual field defect, or both, to a consultant ophthalmologist for consideration of a definitive diagnosis and formulation of a management plan.
- People with a diagnosis of OHT, suspected COAG or COAG should be monitored and treated by a trained healthcare professional who has all of the following: - a specialist qualification (when not working under the supervision of a consultant ophthalmologist)
 - Relevant experience
 - Ability to detect a change in clinical status

Provision of Information

Offer people the opportunity to discuss their diagnosis, prognosis and treatment, and provide them with relevant information in an accessible format at initial and subsequent visits. This may include information on the following:

- Their specific condition (OHT, suspected COAG and COAG), its life-long implications and their prognosis for retention of sight
- That COAG in the early stages and OHT and suspected COAG are symptomless
- That most people treated for COAG will not go blind
- That once lost, sight cannot be recovered
- That glaucoma can run in families and that family members may wish to be tested for the disease
- The importance of the person's role in their own treatment – for example, the ongoing regular application of eye drops to preserve sight
- The different types of treatment options, including mode of action, frequency and severity of side effects, and risks and benefits of treatment, so that people are able to be active in the decision-making process
- How to apply eye drops, including technique (punctal occlusion and devices) and hygiene (storage)
- The need for regular monitoring as specified by the healthcare professional
- Methods of investigation during assessment
- How long each appointment is likely to take and whether the person will need any help to attend (for example, driving soon after pupil dilatation would be inadvisable)
- Support groups
- Compliance aids (such as dispensers) available from their General Practitioner or community pharmacist
- Letter of Vision Impairment (LVI), Referral of Vision Impairment (RVI) and Certificate of Vision Impairment (CVI) registration
- Driver and Vehicle Licensing Agency (DVLA) regulations

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Clinical Algorithm
Foreign Language Translations
Patient Resources
Quick Reference Guides/Physician Guides
Resources
Slide Presentation
Staff Training/Competency Material

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Center for Acute Care. Glaucoma. Diagnosis and management of chronic open angle glaucoma and ocular hypertension. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Apr. 37 p. (NICE clinical guideline; no. 85).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2009 Apr

GUIDELINE DEVELOPER(S)

National Collaborating Centre for Acute Care - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Guideline Development Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All members of the Guideline Development Group and all members of the National Collaborating Centre for Acute Care staff were required to make formal declarations of interest at the outset, and these were updated at every subsequent meeting throughout the development process. No interests were declared that required actions. See Appendix B of the full version of the guideline document for all declarations of interest.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Glaucoma. Diagnosis and management of chronic open angle glaucoma and ocular hypertension. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence; 2009 Apr. 15 p. (Clinical guideline; no. 85). Electronic copies: Available in Portable Document Format (PDF) from the [NICE Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0845 003 7783 or e-mail publications@nice.org.uk. ref: N1846.

- Glaucoma. Diagnosis and management of chronic open angle glaucoma and ocular hypertension. Full guideline. London (UK): National Institute for Health and Clinical Excellence; 2009 Apr. 260 p. (Clinical guideline; no. 85). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Glaucoma: diagnosis and management of chronic open angle glaucoma and ocular hypertension. Costing report. Implementing NICE guidance. London (UK): National Institute for Health and Clinical Excellence; 2009 Apr. 39 p. (Clinical guideline; no. 85). Electronic copies: Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Glaucoma. Costing template. Implementing NICE guidance. London (UK): National Institute for Health and Clinical Excellence; 2009. Various p. (Clinical guideline; no. 85). Electronic copies: Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Glaucoma. Implementing NICE guidance. Slide set. London (UK): National Institute for Health and Clinical Excellence; 2009. 20 p. (Clinical guideline; no. 85). Electronic copies: Available in Portable Document Format (PDF) from the [NICE Web site](#).
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- Service for people at risk of developing glaucoma. Commissioning guide. London (UK): National Institute for Health and Clinical Excellence; 2009. Various p. (Clinical guideline; no. 85). Electronic copies: Available from the [NICE Web site](#).
- Glaucoma. An online educational tool. London (UK): National Institute for Health and Clinical Excellence; 2009. Various p. (Clinical guideline; no. 85). Electronic copies: Available from the [NICE Web site](#).
- Glaucoma guideline: clarification on the eye pressure measurement recommendation. London (UK): National Institute for Health and Clinical Excellence; 2009. Various p. (Clinical guideline; no. 85). Electronic copies: Available from the [NICE Web site](#).
- The guidelines manual 2007. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 April. Electronic copies: Available in Portable Document Format (PDF) from the [NICE Web site](#).

PATIENT RESOURCES

The following is available:

- Diagnosing and treating glaucoma and raised eye pressure. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence; 2009 Apr. 11 p. (Clinical guideline; no. 85). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#). Also available in Welsh from the [NICE Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0845 003 7783 or e-mail publications@nice.org.uk. ref: N1847.

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